REMARKS

I. Claim Status

Claims 1-99 have been cancelled without prejudice to further prosecution in one or more related continuation or divisional applications. Claims 300-427 have been added to claim specific array-based embodiments of the present invention. In the January 3, 2003 Office Action, the Examiner indicated that the election of species requirement was withdrawn. To the extent the species election applies to the new claims, Applicants wish to point out that claims 300-312, 314-332, 334-352, 354-373, and 375-427 are readable on the elected species of a physical array. Upon entry of the present Amendment, claims 300- 427 are pending.

Support for the new claims can be found throughout the Specification and figures, as well as in the original claims (in particular the elected Group I claims 1-99). Support for element (a) can be found in the Specification at page 63, lines 25 to page 64, line 8. Support for elements (b), (c), and (d) in the new claims can be found in the Specification at, *inter alia*, page 148, lines 13-16; page 92, line 1 to page 93, lines 10; page 4, lines 9-16; page 39, lines 6-19; page 63, lines 1-6; and original claim 4. Support for the detector element in the new claims can be found in the Specification at page 40, line 29 to page 41, line 5; at page 130, line 18 to page 131, line 26. Support for the liquid phase array claim element in the system can be found in the Specification at page 36, lines 17-24, and original claim 8. Support for the automated fragmentation module, oligonucleotide synthesizer, and fragmentation purification element can be found in the Specification at, for example, page 81, line 1 to page 85, line 2. Support for claims 314-316, 334-336, 354-356, 375-377, 386-387, 397-398, 406-407, and 416-417 can be found in the Specification at, for example, page 63, line 25 to page 64, line 6; original claim 92. Support for claims 303, 323, 343, 363, 384, 394, 404, and 415 can be found in the Specification at, for example, page 75, lines 5-8. Support for the product production and purification modules can be found in the Specification at, for example, Figure 1A; page 108, line 27 to page 147, line 25; original claim 65. New claims 421-427 find support in original claim 3. Accordingly, it is respectfully submitted that no new matter is introduced by entry of the subject amendments as the amendments and new claims are fully supported by the specification and original claims.

II. Objection to Specification

Applicants respectfully request withdrawal of the objection to the Specification which has been amended to delete the embedded hyperlinks.

III. Rejection under 35 U.S.C. § 112, 2nd Paragraph

Claim 17 has been rejected under 35 U.S.C. § 112, 2nd paragraph, as being indefinite for lack of antecedent basis with respect to the recitation of a shuffling or mutagenesis module. This rejection has been rendered moot by the cancellation of claim 17.

IV. Rejection under 35 U.S.C. § 102(e)

The Examiner's rejection of claims 1, 2, 6-11, 12, 13, 97, 98 and 99 under 35 U.S.C. 102(e) as being allegedly anticipated by the Chetverin et al. patent is respectfully traversed in view of the new claims.

The Chetverin et al. patent is cited for allegedly teaching a method of protein engineering in which amplified mutant strands are transcribed and translated, using components for cell free translation, in an array. The Chetverin et al. patent is generally directed to solid phase oligonucleotide arrays, where each immobilized oligonucleotide has two sequence segments, one variable and the other constant. The arrays are described as being useful for sorting strands according to their terminal ends. (see, e.g., col. 3, line 45 to col. 4, line 5)

The present invention is directed to a system for generating diverse nucleic acids and polypeptides. In contrast to the present invention, as defined by the new claims, Chetverin et al. do not describe Applicants' system, which has among other elements, a computer that contains data corresponding to either target sequences for diversity generation or diverse sequences. Chetverin et al. likewise do not describe or suggest the purification of polypeptide product produced from diverse nucleic acids such as those generated by the claimed system (see claims 360-380). They also do not describe a system having the elements of a liquid phase array as claimed in claims 381-420. Accordingly, the Chetverin et al. patent cannot be found to anticipate Applicants' invention and withdrawal of this rejection is respectfully requested.

V. Rejections under 35 U.S.C. § 103

A. The Chetverin et al. patent, in view of the Nova et al. patent

Claim 2 stands rejected under 35 U.S.C. § 103(a) over the Chetverin et al. patent, in view of the Nova et al. patent (USP 6,284,459). Applicants believe that the Examiner meant this rejection to be applied against claim 3, which is directed to bar codes, rather than claim 2. As both of these claims have been cancelled, Applicants will traverse the rejection in view of new claims 421-427 which are directed to a bar-code reader for sample tracking.

The Office Action alleges that one of ordinary skill in the art would have been motivated to apply bar codes to Chetverin reaction wells in order to maintain identity and content information. The Nova et al. patent is generally directed to the use of matrix materials that are encoded with an optically readable code. (See Abstract) A number of applications for the matrix materials is described, though no where do Nova et al. describe or suggest the specific combination of Applicants' claim elements for generating diversity in biological molecules. At most, Nova et al. describe the usefulness of the matrix materials in connection with various equipment and in various singular operations. Absent however is a suggestion of Applicants' claimed combination of system elements, such as, for example, a computer having data that corresponds to either target sequences for diversity generation or diverse sequences, and a product production module operably coupled to a product purification module. Because the Nova et al. patent does not provide any suggestion for combining elements as Applicants have, the Nova et al. patent fails to cure the deficiencies of the Chetverin et al. patent described above. Further, because the combination of the Chetverin et al. and Nova et al. patents does not provide all the limitations of Applicants' invention, it cannot then serve as a basis for establishing a prima facie case of obviousness Accordingly, Applicants respectfully ask that the rejection be withdrawn.

B. The Patten et al. patent, in view of the Iverson et al. patent

Claims 1, and 3-99 stand rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over the Patten et al. patent, U.S. Pat. No. 6,406,910, in view of the Iverson et al. patent, U.S. Pat. No. 6,180,341. This rejection is traversed in view of the new claims.

The Patten et al. patent is relied upon for describing in vitro evolution and in vitro transcription and translation, as well as some generic robotic systems. The present invention is

directed to a specific combination of automated elements for the generation of nucleic acid diversity, beginning with a computer containing specific data for facilitating the automated generation of diverse nucleic acids through the automated production of polypeptide product. In contrast to the Patten et al. patent, the present invention provides for the automated purification of polypeptide product (i.e., claims 300-380) and the specific use of liquid phase arrays in certain specific embodiments (i.e., claims 381-420).

The Iverson et al. patent is cited for describing in vitro mutagenesis in a physical array of microtiter plate for high throughput mutagenesis. However, Iverson et al. provide no description or suggestion of what part of their method one would improve upon to achieve Applicants' invention. The Iverson et al. patent characterizes the method that is described as already being "high throughput" by virtue of the combination of mutagenesis and in vitro transcription and translation. (See Abstract) Hence there is no motivation provided by the combination of the Patten et al. patent and the Iverson et al. patent for combining the two references together. Even if the combination were proper, it is unclear why or how, for example, one would utilize a computer in the combined teachings of these patents. Likewise, the cited references provide no motivation for automating polypeptide production and operably coupling it to a purification operation. Accordingly, withdrawal of this rejection is respectfully requested.

C. The Patten et al. patent, in view of the Iverson et al. patent, further in view of the Nova et al. patent

Claim 2 stands rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over the Patten et al. patent, in view of the Iverson et al. patent, and in further view of the Nova et al. patent. For the reasons stated in part A above, this rejection is respectfully traversed in view of new claims 421-427 which are directed to a bar-code reader for sample tracking.

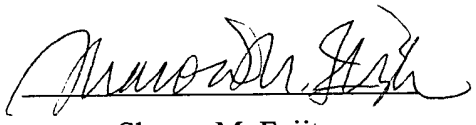
Although the Nova et al. patent does describe sample tracking, it does not provide any motivation for combining any of the pieces of equipment or labware described in either the Patten et al., Iverson et al., or Nova et al. patents into a system for diversity generation that is identical to Applicants' claimed system. Thus, it does not cure the deficiencies of the Patten et al. or Iverson et al. patents, taken either alone or in combination. Accordingly, Applicants respectfully ask that this rejection be withdrawn.

CONCLUSION

In light of the foregoing amendments and remarks, Applicants believe that all pending claims are allowable and respectfully request a Notice of Allowance for this application from the Examiner. Should the Examiner believe that a telephone conference would expedite the prosecution of this application, the undersigned can be reached at the telephone number set out below. The Commissioner is hereby authorized to charge any fee deficiencies in connection with this submission to Deposit Account No. 50-0990.

Respectfully submitted,

July 3, 2003

By: 

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